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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,067	10/04/2004	Craig W. Lindsley	21078YP	5618

210 7590 09/25/2006

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,067	LINDSLEY ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,11-17,23 and 24* is/are rejected.

7)☒ Claim(s) *4-7,9 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/20/04&4/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The abstract of the disclosure is objected to because it does not convey a structural makeup. Correction is required. See MPEP § 608.01(b).

Claims 1-3,8,11-14,17,23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The nature of "optional" substituents for benzyl in R_b is not set forth in the claims nor is it seen in the specification as far as the examiner can determine.

2. Claims 13-15 are unclear as to intended scope. Such claim language reciting inhibitory activity is generally used to denote a causative factor in determining the process by which a particular disease occurs. Determining whether a given disease responds or not to inhibition of "one or more of the isoforms of Akt" involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

Claims 1-3, 8 ,11-17 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1).Specification is not adequately enabled by way of working examples for the scope of bis-phenyl compounds claimed which are not even limited to a particular azine core but can include up to 5 N atoms in the bicycle ring system which can have a variety of heterocyclic groups including fused rings and substituted derivatives thereof at all R variables.It is stated in the specification on p.70 that: "Compounds of the instant invention described in Scheme 1 and Table 1 were tested in the assay…". Said compounds are always quinoxalines with R6 being lower alkyl, aromatic carbocyclic, haloalkyl, cycloalkyl with 1 example each of a hetero rings, namely thienyl, thiazolyl with N-acetyl substituent and quinolinyl. The second phenyl ring is unsubstituted as is the benzene portion of the quinoxaline ring. Thus, there is no reasonable basis for assuming that the myriad of remaining compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the

same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the millions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as the compounds are taught to act as inhibitors of Akt activity of which there are many forms . It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- as stated above only a small portion of instant scope has been tested as stated on p.70;

4) State of the prior art- The compounds are 2,3-diphenyl quinoxalines as well as quinolines,naphthyridines and a myriad of other fused azine ring systems with sulfonylaminoalkyl substitution on one of the phenyl rings . No such

compounds are known in the prior art directed to exemplified species much less having the instant activity;

5) Working examples- No actual test data has been presented only an upper limit is reported on p.70 and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

2.) Method claims 11-16 and 23-24 are also rejected herein for the following reasons. Treating cancer is not enabled solely on the reliance of assay testing for inhibition of the activity of one or more isoforms of AKT. While AKT inhibition may be implicated in the development of certain cancers as discussed in the references, Nakatani and Bellacosa, there is no basis in the prior art at the time of applicants' effective filing that any AKT inhibitor much less as a class are known to treat all cancers. Note Hanada, a more recent publication, evidences that research in this area is in the preliminary stages. Note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Level of unpredictability in the art- The invention is pharmaceutical in nature involving inhibition of one or more kinases of which many types currently

exist with differing biological functions as discussed in Nakatani and Bellasco. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18. ;

2) Direction or guidance- The amount of guidance presented in the specification as to which compounds are sufficiently active to be useful for the claimed uses is nonexistent;

3) Working examples- The test data presented is for an assay testing which is not art-recognized as being reasonably predictive of *in vivo* efficacy. Thus in the absence of animal studies and in the absence of any correlation between studies conducted **in vitro** and the diseases to be treated, there is no sufficient evidence to support the claimed uses;

4) Level of skill in the art- The area directed to PKT inhibition is very experimental with no indication of any such drug(s) actually known to treat one or more cancers and thus the level of skill is low. If applicants disagree they need to provide references showing at the time of applicants' filing date one or more cancers described herein would be reasonably treatable in man, the intended host with Akt inhibitors.

Where the assertion of utility is unusual, difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of in vivo efficacy by those skilled in the art. See for example, In re Ruskin 148 USPQ 221; Ex parte Jovanovics 211 USPQ 907. Note MPEP. 2164.05(a).

In view of the above considerations, this rejection is being applied.

Claims 4-7 and 9-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624